Zai Lab Announces The New England Journal of Medicine Publication Demonstrating Durable Clinical Activity of Repotrectinib in Patients with Advanced ROS1 Fusion-Positive NSCLC

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Phase 1/2 TRIDENT-1 study data demonstrate repotrectinib's clinically meaningful response rates and durable clinical activity in patients with ROS1-positive non-small cell lung cancer

Data show robust intracranial activity both in TKI naïve and pretreated settings in patients with ROS1-positive NSCLC

Findings demonstrate potential of repotrectinib to overcome limitations of first-generation TKIs in terms of durability of responses and activity in ROS1 resistance mutations

TRIDENT-1 study ongoing globally; Zai Lab leading execution in Greater China

SHANGHAI & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 10, 2024-- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688) today announced *The New England Journal of Medicine (NEJM)* has published data from the registrational Phase 1/2 TRIDENT-1 study evaluating repotrectinib (TPX-0005) in patients with *ROS1* fusion-positive (*ROS1*+) non-small cell lung cancers (NSCLCs). Repotrectinib is a tyrosine kinase inhibitor (TKI) that has shown robust anti-tumor activity against *ROS1*+ cancers in preclinical models. In the TRIDENT-1 study, repotrectinib demonstrated high response rates and durable activity in patients with *ROS1*+ NSCLC, including patients with TKI-naïve and TKI-pretreated tumors, *ROS1* G2032R resistance mutations and brain metastases. Treatment with repotrectinib was generally well tolerated with a manageable safety profile compatible with long-term administration.

Turning Point Therapeutics, a wholly owned subsidiary of the Bristol-Myers Squibb Company, sponsored and designed the global, registrational TRIDENT-1 study. In August 2022, Bristol Myers Squibb acquired the company, including its asset repotrectinib. As part of its exclusive license agreement with Turning Point Therapeutics to develop and commercialize repotrectinib in Greater China (mainland China, Hong Kong, Taiwan, and Macau), Zai Lab participated and enrolled 81 patients for this trial.

Every year in China, more than 800,000 people are newly diagnosed with lung cancer, and NSCLC accounts for approximately 85% of the cases. *ROS1* rearrangements occur in ≤2% of patients with NSCLC[1]. Brain metastases are common among patients with *ROS1*+ NSCLC and intracranial activity of approved ROS1 TKIs can be suboptimal.

"The results from the TRIDENT-1 study suggest repotrectinib results in high and durable response rates in patients with *ROS1*+ NSCLC, in the settings of both treatment naïve, treatment resistant, and intracranial disease, which may address the limitations of first-generation TKIs," said Rafael G. Amado, M.D., president, head of Global Oncology Research and Development, Zai Lab. "We look forward to advancing the development of repotrectinib in Greater China as a next generation treatment in this clinical setting."

TRIDENT-1 is a registrational, first-in-human Phase 1/2 study assessing the efficacy and safety of repotrectinib in patients with advanced solid tumors, including *ROS1*+ NSCLC. In the study, 519 patients received one or more doses of repotrectinib, with 103 treated in Phase 1 and 416 treated in Phase 2. Primary endpoints were maximum tolerated dose (MTD) and/or recommended Phase 2 dose (RP2D) and confirmed objective response rate (ORR), as assessed by blinded independent central review (BICR) using RECIST v1.1 (Phase 2). Secondary endpoints included duration of response (DOR), progression-free survival (PFS) and safety.

Based on the results of this trial, the Center for Drug Evaluation (CDE) of the National Medical Products Administration (NMPA) accepted the New Drug Application (NDA) for repotrectinib submitted by Zai Lab for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive NSCLC, after granting priority review in May 2023. In November 2023, the U.S. Food and Drug Administration approved repotrectinib for use in adult patients with locally advanced or metastatic *ROS1*+ NSCLC in the United States.

About Repotrectinib

Repotrectinib is a next-generation tyrosine kinase inhibitor (TKI) targeting the *ROS1* and *NTRK* oncogenic drivers of advanced solid tumors, including non-small cell lung cancer (NSCLC). Patients with tumor harboring *ROS1* and *NTRK* gene fusions treated with approved targeted therapies often develop resistance mutations, eventually leading to tumor progression. Repotrectinib is the first next-generation TKI for *ROS1*-positive metastatic NSCLC and tumors with *NTRK* fusions, uniquely designed to address key drivers of disease progression.

In China, repotrectinib has been granted four Breakthrough Therapy Designations from the Center for Drug Evaluation (CDE) of the National Medical Products Administration (NMPA) in *ROS1*-positive metastatic NSCLC patients who have not been treated with a *ROS1* TKI; *ROS1*-positive metastatic NSCLC patients who have previously been treated with a *ROS1* TKI and who have not received prior platinum-based chemotherapy; *ROS1*-positive metastatic NSCLC patients who have previously been treated with a *ROS1* TKI and one prior line of platinum-based chemotherapy; and patients with advanced solid tumors that have an NTRK gene fusion who have progressed following treatment with prior TRK tyrosine kinase inhibitors (TKIs).

Zai Lab has an exclusive license agreement with Turning Point Therapeutics, a wholly owned subsidiary of the Bristol-Myers Squibb Company, to develop and commercialize repotrectinib in Greater China (mainland China, Hong Kong, Taiwan and Macau).

About Zai Lab

Zai Lab (NASDAQ: ZLAB; HKEX: 9688) is an innovative, research-based, commercial-stage biopharmaceutical company based in China and the United States. We are focused on discovering, developing, and commercializing innovative products that address medical conditions with significant unmet needs in the areas of oncology, autoimmune disorders, infectious diseases, and neuroscience. Our goal is to leverage our competencies and resources to positively impact human health in China and worldwide.

For additional information about Zai Lab, including our products, business activities and partnerships, research, and other events or developments, please visit www.zailaboratory.com or follow us at www.twitter.com/ZaiLab_Global.

Zai Lab Forward-Looking Statements

This press release contains forward-looking statements about future expectations, plans, and prospects for Zai Lab, including, without limitation, statements relating to the prospects of repotrectinib and the potential treatment of NSCLC and NTRK-positive solid tumors in Greater China. These forward-looking statements may contain words such as “aim,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “plan,” “possible,” “potential,” “will,” “would,” and other similar expressions. Such statements constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are not statements of historical fact or guarantees or assurances of future performance. Forward-looking statements are based on our expectations and assumptions as of the date of this press release and are subject to inherent uncertainties, risks and changes in circumstances that may differ materially from those contemplated by the forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including but not limited to (1) our ability to successfully commercialize and generate revenue from our approved products; (2) our ability to obtain funding for our operations and business initiatives, (3) the results of our clinical and pre-clinical development of our product candidates, (4) the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approvals of our product candidates, (5) risks related to doing business in China, and (6) other factors identified in our most recent annual and quarterly reports and in other reports we have filed with the U.S. Securities and Exchange Commission. We anticipate that subsequent events and developments will cause our expectations and assumptions to change, and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

Our SEC filings can be found on our website at www.zailaboratory.com and on the SEC’s website at www.sec.gov.

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[1]Zhang et al. Prevalence of ROS1 fusion in Chinese patients with non-small cell lung cancer, *Thoracic Cancer* January 2019.

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